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Waldenström's Macroglobulinemia in Young African-American Adults

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We have identified five African-American patients with Waldenström's macroglobulinemia (WM) diagnosed at a young age (ages 35, 38, 38, 40, 51; 4 males, 1 female). All had a history of intravenous heroin abuse and four also used cocaine. Their manner of presentation and clinical course were typical. Three of three patients tested for the hepatitis C virus (HCV) were positive and three of three patients tested were HIV negative. The potential relationship between intravenous drug abuse and/or HCV to development of WM in this group of young patients is provocative, especially since a polyclonal increase in serum IgM is commonly seen in chronic intravenous heroin addicts. More recently, the contribution of HCV is being evaluated in lymphoproliferative disorders. Although WM is typically a disease of older people, it should also be considered in the differential in a young patient with a suggestive clinical picture. Am. J. Hematol. 60:229–230, 1999.

Key words: Waldenström's; African-American; IV drug abuse; hepatitis C

INTRODUCTION

Waldenström's macroglobulinemia (WM) is a disease that predominantly affects older caucasians with a median age at diagnosis of 63 years [1]. In an analysis of 151 patients with WM reported to National Cancer Institute's Surveillance, Epidemiology, and End-Results (SEER) program during the period from 1978 to 1989, only four patients were younger than 40 years of age [2]. There were only five African-American women identified with this disease and no cases were reported in African-American men during the study period. In a series of 71 patients reported by Kyle and Garton [3], less than 1% of patients were younger than 40 years. Krajny and Pruzanski [4] reported a 29-year-old patient with WM in his review of 45 cases. The etiology of WM is not well understood and the risk factors for the development of disease at a young age are unclear. We have identified five African-American patients with WM diagnosed at a young age. All had a history of intravenous heroin abuse. Three of three patients tested for the hepatitis C virus (HCV) were positive. The potential relationship between intravenous drug abuse (IVDA) and/or HCV to the development of WM in this group of young patients is discussed.

PATIENTS AND METHODS

Patients were identified by retrospective review of charts from patients referred to the Barbara Ann Karmanos Cancer Institute and Wayne State University and Henry Ford Hospital. For the patients whose diagnosis was made at another institution, slides, medical summaries, and treatment data were obtained for review.

RESULTS

Between 1987 and 1997, five African-American patients with WM diagnosed at a young age were identified (ages 35, 38, 38, 40, 51; 4 males, 1 female). All had a history of intravenous heroin abuse and four also used cocaine. The manner of presentation included bleeding diathesis (one intracranial, one uterine, one rectal, one epistaxis), syncope, generalized weakness, and hyperviscosity. One patient each had their course complicated by

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autoimmune hemolytic anemia and cryoglobulinemia. Four of the five patients had either hepatosplenomegaly or lymphadenopathy during their course and one patient had neither. Laboratory analysis revealed total serum immunoglobulin (Ig)M at diagnosis to be between 2,600 mg/dL and 10,100 mg/dL (2,600, 2,780, 4,150, 10,000, 10,100) and blood hemoglobin between 3.0 gm/dL and 11.8 gm/dL (3.0, 7.2, 7.5, 11.0, 11.8) at diagnosis. Three of three patients tested for HCV were positive and three of three patients tested were HIV negative. Four of five patients were initially treated with an alkylator-based regimen and two patients achieved stable disease (a decrease in measurable tumor mass lesions by a least 25% but <50% and a reduction in serum IgM levels by <50%) and two patients achieved a partial response (a decrease in measurable tumor mass by at least 50% and a reduction in serum IgM levels by at least 50%). All of the patients were treated with a purine analog (three patients with fludarabine; three patients with 2-CdA) and achieved either a partial response (one patient) or stable disease (four patients). Four of five of the patients are alive at 1, 5, 6, and 10 years after diagnosis and one patient expired at 5 years.

DISCUSSION

In a disease with a median age of onset of 63 years, an incidence in patients younger than 40 years between 1–3% [2–4], and a caucasian predominance, we find the identification of five African Americans with early-age onset of WM quite provocative. There are few clues to the etiology of WM. Some studies have shown an association between WM and aberrations of immune function with a few reports showing that some IgM proteins show antibody activity against specific antigens [5]. There is considerable literature suggesting an element of familial susceptibility, including families with multiple cases of WM and IgM monoclonal gammopathy of undetermined significance (MGUS) in first degree relatives of patients with WM [6]. The potential relationship between IVDA and/or HCV to the development of WM in our group of young patients is intriguing. Changes in Ig profile have been reported in intravenous heroin addicts. The most common noted abnormality is an isolated polyclonal hypermacroglobulinemia with normal IgA and IgG that appears to be at least partially reversible upon administration of methadone [7]. Interestingly, patients reporting their route of heroin administration to be intranasal had a very low incidence of IgM serum elevation. Recently, the contribution of HCV is being evaluated in lymphoproliferative disorders. Santini et al. [8] demonstrated the presence of hepatitis C viral replication by polymerase chain reaction in six of six patients with WM tested. More recently, Kaposi's sarcoma-associated herpesvirus (KSHV), a novel member of the herpes-virus family, was detected in the dendritic cells of patients with multiple myeloma, MGUS and WM [9,10]. Further studies are needed to clarify the involvement of both HCV and KSHV in the pathogenesis of lymphoproliferative disorders. Although WM is typically a disease of older people, it should also be considered in the differential in a young patient with a suggestive clinical picture.

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